IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT INTERFERENCES

Moncada :

v. : Interference No. 100,116

Johnson, et al. :

To the Commissioner of Patents and Trademarks

Washington, D. C. 20231

DECLARATION UNDER MPEP 1105.02 IN SUPPORT OF JOHNSON MOTION TO DISSOLVE

UDO F. AXEN, being duly warned that willful false statements and the like are punishable by fine or imprisonment or both (18 USC 1001) and may jeopardize the validity of the Johnson, et al. application of the above-captioned interference or any patent issuing thereon, states and declares:

THAT all statements herein made of his own knowledge are true and that all statements herein made on information and belief are believed to be true;

THAT he is an organic chemist, having received the Dr. rer. nat. degree from the University of Bonn in 1963;

THAT since 1966 he has been employed by The Upjohn Company, Kalamazoo, Michigan, in the Experimental Chemistry Department;

THAT he is presently Research Manager, Experimental Chemistry I;

THAT, during his employment with The Upjohn Company, he has had extensive personal involvement in the prostaglandin research programs of The Upjohn Company;

THAT since 1976 he has been involved in the research programs of The Upjohn Company relating to the discovery of prostacyclin, including the various discoveries made within the Experimental Chemistry Research Department of The Upjohn Company described in the Johnson application in the above-captioned interference;

THAT he is further personally familiar with the relationship which has developed between Upjohn and the Wellcome Foundation Ltd. regarding the discovery of prostacyclin and related discoveries;

THAT he has read the contents of the file wrapper of the Moncada application in the above-captioned interference and the Preliminary Statement of the party Moncada in the above-captioned interference;

THAT he is further familiar with the subject matter of the count of the above-captioned interference;

THAT the information contained in the Moncada file wrapper and Preliminary Statement, including the exhibits attached thereto, is in general terms consistent with his understanding of the discovery and development by Moncada and others at the Wellcome Foundation of prostacyclin;

THAT with respect to the United Kingdom applications on

which Moncada relies for priority (Nos. 19384, 34151, 36547, filed respectively 11 May, 17 August, and 3 September 1976), each of these alleged priority applications describes a method for a preparation of a residue designated as "PGX", which is prepared by incubation in certain microsomes in a tris buffer, followed by extraction in cold dry diethyl ether and concentration to a residue;

THAT Moncada's first alleged priority application describes, by Moncada's later admission, an incorrect tentative structure for the residue, i.e., the PGX product of the Moncada process, namely the 5-hydroperoxide structure therefor;

THAT the PGX product of the Moncada process in these priority applications is now characterized by Moncada at pages 4-5 of his Preliminary Statement as a complex mixture of various substances, one of which is prostacyclin, where Moncada states in conclusion:

> "On evaporation to dryness of the [diethyl] ether extract there was obtained a powdery residue which would have consisted of prostacyclin and these [tris and sodium] salts."

THAT, however, as of late June, 1976, the character of the PGX product of the Moncada process was unknown to Moncada or the Wellcome Foundation, as is evidenced by page 4 of Exhibit F of the Moncada Preliminary Statement where the Wellcome minutes of a meeting with Upjohn representatives

indicates the following:

> "Dr. Vane indicated that Wellcome is interested in obtaining Upjohn help and assistance in identifying PGX and its analogs so that stable compounds can be developed with activity in the treatment areas indicated by D. ...
>
> "Dr. Weisblat indicated that Upjohn would like to identify PGX and to this end will furnish Wellcome some compounds which have already been made."

THAT in July of 1976, as indicated in the Moncada Preliminary Statement, scientists from the Wellcome Foundation prepared the PGX product of the Moncada process in the Research Laboratories of The Upjohn Company in Kalamazoo, Michigan;

THAT these activities indicate to him that as of July, 1976, Moncada had prepared from biological sources a residue containing a complex mixture of products of essentially unknown character or structure and had assigned as the name of that residue, or the supposed active principle thereof, "PGX";

THAT, in contrast to the biological preparation of products consisting of complex mixture of substances, scientists at The Upjohn Company, particularly the inventors of the Johnson application of the above-captioned interference and those working at their direction and control, prepared novel organic compounds within the scope of the count of the above-captioned interference, namely analogs and/or derivatives of prostacylcin;

THAT these substances were essentially contemporaneously characterized and essentially chemically pure organic compounds, the first of which was the preparation of prostacyclin methyl ester or PGI_2 methyl ester on or about 7 July 1976;

THAT subsequent to the preparation of prostacyclin methyl ester, on or about 2 August 1976 prostacyclin sodium salt (PGI_2 sodium salt) as a free-flowing white (presumably crystalline) solid was prepared by those working under the direction and control of the inventors of the Johnson application;

THAT, subsequent to the preparation of prostacyclin sodium salt, on or about 3 August 1976 experiments were performed in the Research Laboratories of The Upjohn Company which indicated that at least one component of the PGX product of the Moncada process could be esterified to a substance substantially chemically identical to prostacyclin methyl ester;

THAT, within his information and belief, this is the first scientific proof of a connection between the invention of the PGX product of the Moncada process and the invention of Johnson, et al. in derivatives and analogs of prostacyclin;

THAT the demonstration of the chemical equivalence of an esterified PGX product of the Moncada process with

prostacyclin methyl is reported in the accompanying declaration of R. A. Johnson;

THAT this demonstrated equivalence in his opinion was then and is now strong evidence that the novel biologically active principle of PGX product of the Moncada process was at least in part, if not preponderantly prostacyclin; and

THAT, in his opinion, this discovery of prostacyclin by Moncada, i.e., the discovery of the PGX product of the Moncada process, was a separate and independent scientific discovery from the invention by Johnson, et al. of prostacyclin derivatives, specifically prostacyclin esters and prostacyclin salts;

THAT, in his opinion, the scientific connection between these discoveries was established only retrospectively, in that the identity of the novel biologically active principle of the PGX product of the Moncada process to the free acid form of prostacyclin was established only after the respective inventions of Moncada and Johnson, et al. had been made;

THAT commencing in mid-1976, he began an extensive relationship with Dr. N. Whittaker of the Wellcome Foundation Ltd., regarding the prostacyclin research programs being undertaken within the Experimental Chemistry Research Department of The Upjohn Company;

THAT as a part of the relationship betwen Dr. N. Whittaker and the research personnel of The Upjohn Company,

certain confidential information was disclosed to Dr. N. Whittaker prior to 1 July 1976, including a method for preparing prostacyclin chemically;

THAT this confidential disclosure to Dr. N. Whittaker is recorded in the memorandum attached hereto as Exhibit A, wherein prostacyclin is indicated thereon as "enol ether - not isolated";

THAT he personally delivered a 100 mg sample of prostacyclin sodium salt to Dr. N. Whittaker in Boston, Massachusetts, on 23 August 1976, as indicated by Exhibit B, attached hereto;

THAT prior to 29 November 1976 additional prostacyclin sodium salt was, on his information and belief, sent to the Wellcome Foudnation Ltd.;

THAT he has read the Moncada Preliminary Statement at pages 12-13, where Moncada states:

> "On 29th November, 1976, on information and belief, the said Dr. N. Whittaker landed at Los Angeles, United States of America, with a sample of crystalline prostacyclin sodium salt. ... He gave this sample of prostacyclin sodium salt to the said Dr. David Weisblat The Upjohn Company ...";

THAT, in his opinion and on his information and belief, the sample of prostacyclin sodium salt referred to in the Moncada Preliminary Statement was prepared by Dr. N. Whittaker or under his direction by purely chemical means and not by biological means;

THAT, in his opinion and on his information and belief, this sample of prostacyclin sodium salt was not prepared from the PGX product of the Moncada process;

THAT, in his opinion, the ability of Dr. N. Whittaker, or those acting under his direction or control, to prepare such a sample of prostacyclin sodium salt was derived either in whole or in part from the aforementioned-disclosures and samples (e.g. evidenced by Exhibits A and B attached hereto); and

THAT, therefore, he attributes the sample delivered by Dr. N. Whittaker to the work described in the Johnson application and not to the invention as described by the alleged priority applications of Moncada.

Udo F. Axen

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Date: June 12, 1979